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December 22, 2020
Contains TSCA Confidential Business Information within brackets { }
Sanitized Copy

TSCA Confidential Business Information Center (7407M)
EPA East – Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Subject: Notice in Accordance with TSCA Section 8(e): Submission of study reports that meet the criteria for TSCA 8(e)

Dear Sir/Madam,

{ }, submits this letter under section 8(e) of the Toxic Substances Control Act (TSCA) to inform the U.S. Environmental Protection Agency (EPA) of the results of toxicity testing with an early-stage experimental pesticide being screened for potential registration and development in the United States.

{ } understands that reporting of results from this study under TSCA 8(e) is in accordance with EPA's policy. { } has not made a determination at this time that any substantial risk of injury to human health or the environment is presented by the findings within the subject study.

Please note that a confidential version of this letter is enclosed, treating the chemical identity and company identity as Confidential Business Information.

A Confidentiality Substantiation Questionnaire is being submitted.

If you have any questions with regard to this submission, please contact me at { }.

Sincerely,

{ }

TEST SUBSTANCE: { }

STUDY No.: { }
TITLE: A GLP 28 Day Oral (Dietary) Study of { } in CD-1 Mice

{ } recently learned new toxicological effects in a repeated oral toxicity study using mice. An outline of the study is as follows:

STUDY OUTLINES AND COMMENTS

{ } was orally administered via the diet to mice repeatedly at dose levels of 200, 800 and 3500 ppm for 28 days.

The following findings { } are reportable under TSCA 8(e).

1. No-observable-adverse-effect-level (NOAEL) was 800 ppm (male; 109 mg/kg/day, female; 145 mg/kg/day) for both sexes.

These results meet the criteria of NOAEL in TSCA 8(e).

STUDY METHOD AND RESULTS

PERFORMING LABORATORY: { }

STUDY METHODS:

Test substance: { }
Animals: Mice, Crl:CD-1 (ICR), males and females, 10 animal / sex / group
Animal age at start of the study: 8 weeks old
Body weight range at start of study: 21.4 – 40.2 g
Administration route: Oral (dietary)
Dose levels: 0, 200, 800 and 3500 ppm
(average test substance intake was 29, 109 and 610 mg/kg/day for males, and 41, 145 and 657 mg/kg/day for females)
Vehicle: basal diet
Treatment period: 28 days
Observation items: Mortality, clinical signs, detailed clinical observation, body weight, body weight gain, food consumption, motor activity, hematology, blood biochemistry, organ weight, necropsy, histopathological examination

RESULTS:

Changes which were indicative of anemia such as lower hemoglobin, and hematocrit were observed in males and females at 3500 ppm. In addition, adverse effects on liver (higher ALP, ALT and SDH, increased relative liver weight and hepatocellular necrosis with the hepatocellular hypertrophy) were noted in males and females at 3500 ppm. Based on the results, the NOAEL of { } was considered to be 800 ppm (male; 109 mg/kg/day, female; 145 mg/kg/day).

(Completed)

TEST SUBSTANCE: { }

STUDY No. { }
TITLE: Oral gavage embryo-fetal development study with { } in rats

{ } recently learned new toxicological effects in an embryo-fetal development study using rats. An outline of the study is as follows:

STUDY OUTLINES AND COMMENTS
Maternal rats were administered with { } orally by gavage during days 6 to 20 of gestation at dose levels of 20, 60 and 200 mg/kg.

In maternal animals, increased liver weights with histopathological changes and effects on hematology parameters (lower hemoglobin and hematocrit) were observed at ≥60 mg/kg/day. Therefore, NOAEL for maternal animals in this study was considered to be 20 mg/kg. (In the case of oral study with the dosing period shorter than 4 weeks, it is reportable when NOAEL is below 200 mg/kg.)

STUDY METHOD AND RESULTS
PERFORMING LABORATORY: { }

STUDY METHODS:
Test substance: { }
Animals: Crl:CD(SD) rat, 24 pregnant animals/group
Animal age at start of the study: 11 to 12 weeks old
Body weight range at start of study: 217 to 268 g
Administration route: orally by gavage
Dose levels: 0, 20, 60 and 200 mg/kg
Vehicle: 0.5% aqueous methylcellulose solution
Treatment period: days 6 to 20 of gestation
Observation items: clinical sign, body weight, body weight gain, food consumption, gross necropsy, gravid uterine weight, organ weights (liver, spleen and thyroid), hematology, histology, caesarean section, thyroid hormone, and observation of live fetuses (anogenital distance, external, visceral and skeletal examination)

RESULTS:
In maternal animals, increased liver weight which correlated with microscopic finding of centrilobular hepatocyte hypertrophy and the effects on hematology parameters (lower hemoglobin and hematocrit) were observed at ≥60 mg/kg. In addition, focal subcapsular (hepatocyte) necrosis was observed in animals administered 60 or 200 mg/kg.
In embryos/fetuses, no adverse effects were observed at any dose levels.

(Completed)

TEST SUBSTANCE: { }
STUDY No.: { }
TITLE: One month oral toxicity study of { } in dogs

{ } recently learned new toxicological effects in a repeated oral toxicity study using dogs. An outline of the study is as follows:

STUDY OUTLINES AND COMMENTS

{ } was administered orally via capsules to Beagle dogs at dose levels of 10, 30 and 100 mg/kg/day for one month.

1. Tremor and ataxic gait were observed in both sexes at 30 and 100 mg/kg/day.
2. No-observed-adverse-effect-level (NOAEL) was considered to be 10 mg/kg/day for both sexes.

Based on the NOAEL (<200 mg/kg/day in an oral study of ≤4 weeks) and the neurotoxic signs, these effects observed in this study are reportable under TSCA 8(e).

STUDY METHOD AND RESULTS

PERFORMING LABORATORY: { }.

STUDY METHODS:

Test substance: { }
Animals: Beagle dogs, males and females, 1 animal/sex/group
Animal age at start of the study: 5 months old
Body weight range at start of study: males; 7.65 - 8.59 kg, females; 7.75 – 8.14 kg
Administration route: Oral
Dose levels: 10, 30 and 100 mg/kg/day
Vehicle: Capsule
Treatment period: One month
Observation items: clinical signs, body weight, food consumption, urinalysis, ophthalmology, hematology, blood biochemistry, organ weight, necropsy, histopathological examination

RESULTS:

No treatment-related changes other than the above were observed.

Based on the neurotoxicity at ≥30 mg/kg/day in both sexes, the NOAEL was considered to be 10 mg/kg/day for both sexes.

TEST SUBSTANCE: { }
STUDY No.: { }
TITLE: Two-week oral toxicity study of { } in mice

{ } recently learned new toxicological effects in a repeated oral toxicity study using mice. An outline of the study is as follows:

STUDY OUTLINES AND COMMENTS

{ } was administered repeatedly to mice (6 animals/sex/group) via the diet at dose levels of 75, 150 and 350 ppm for two weeks.

No-observed-adverse-effect-level (NOAEL) was considered to be 75 ppm (12.3 mg/kg/day) in males and 150 ppm (27.1 mg/kg/day) in females.

Based on the NOAEL (<200 mg/kg/day in an oral study of ≤4 weeks), these effects observed in this study are reportable under TSCA 8(e).

STUDY METHOD AND RESULTS

PERFORMING LABORATORY: { }

STUDY METHODS:

Test substance: { }
Animals: Mice, Crl:CD1(ICR), males and females, 6 animals/sex/group
Animal age at start of the study: 5 weeks old
Body weight range at start of study: male; 24.2-28.9 g, female; 20.1-22.7 g
Administration route: Oral (dietary)
Dose levels: 0, 75, 150 and 350 ppm (12.3, 24.9 and 55.7 mg/kg/day for male and 14.0, 27.1 and 60.6 mg/kg/day for female)
Vehicle: none
Treatment period: two weeks
Observation items: clinical signs, body weight, body weight gain, food consumption, hematology, blood biochemistry, necropsy, organ weight, histopathological examination

RESULTS:

In clinical signs, vocalization was observed at 350 ppm in both sexes. At ≥ 150 ppm in males and 350 ppm in females, an effect on the liver (increase in relative liver weight and centrilobular hepatocyte hypertrophy and higher ALT and AST in both sexes, and single cell necrosis and fine vacuolation in males at 350 ppm) was also observed.

Therefore, NOAEL was determined to be 75 ppm (12.3 mg/kg/day) in males and 150 ppm (27.1 mg/kg/day) in females.

(Completed)

TSCA 8(e) Substantiation Questions

1. Is your company asserting this confidential business information (CBI) claim on its own behalf? **Yes.** If the answer is no, please provide company name, address and telephone number of entity asserting claim.
2. For what period do you assert your claim(s) of confidentiality? If the claim is to extend until a certain event or point in time, please indicate that event or time period. Explain why such information should remain confidential until such point. **This is a research lead that has not been patented and is considered a trade secret. The substance is an early stage experimental pesticide being screened for potential registration and development in the United States. Disclosing research leads before the patent issues could allow competitors to understand our research direction in a highly competitive business.**
3. Has the information that you are claiming as confidential been disclosed to any other governmental agency, or to this Agency at any other time? Identify the Agency to which the information was disclosed and provide the date and circumstances of the same. Was the disclosure accompanied by a claim of confidentiality? If yes, attach a copy of said document reflecting the confidentiality agreement.
4. Briefly describe any physical or procedural restrictions within your company relating to the use and storage of the information you are claiming CBI.
5. If anyone outside your company has access to any of the information claimed CBI, are they restricted by confidentiality agreement(s). If so, explain the content of the agreement(s).
6. Does the information claimed as confidential appear or is it referred to in any of the following:
   a. Advertising or promotional material for the chemical substance or the resulting and product;
   b. Material safety data sheets or other similar materials (such as technical data sheets) for the substance or resulting end product (include copies of this information as it appears when accompanying the substance and/or product at the time of transfer or sale);
   c. Professional or trade publications; or
   d. Any other media or publications available to the public or to your competitors.
   If you answered yes to any of the above, indicate where the information appears, include copies, and explain why it should nonetheless be treated as confidential.
7. Has EPA, another federal agency, or court made any confidentiality determination regarding information associated with this substance? **No**. If so, provide copies of such determinations.
8. Describe the substantial harmful effects that would result to your competitive position if the CBI information is made available to the public? In your answer, explain the causal relationship between disclosure and any resulting substantial harmful effects. Consider in your answer such constraints as capital and marketing cost, specialized technical expertise, or unusual processes and your competitors access to your customers. Address each piece of information claimed CBI separately. **Disclosing research leads before the**

patent issues could allow competitors to understand our research direction in a highly competitive business.

9. Has the substance been patented in the U.S. or elsewhere? Is a patent for the substance currently pending?
10. Is this substance/product commercially available and if so, for how long has it been available on the commercial market?
    a. If on the commercial market, are your competitors aware that the substance is commercially available in the U.S.?
    b. If not already commercially available, describe what stage of research and development (R&D) the substance is in, and estimate bow soon a market will be established.
    c. What is the substance used for and what type of product(s) does it appear in.
11. Describe whether a competitor could employ reverse engineering to identically recreate the substance? **This is possible.**
12. Do you assert that disclosure of this information you are claiming CBI would reveal:
    a. confidential processes used in manufacturing the substance;
    b. if a mixture, the actual portions of the substance in the mixture; or
    c. information unrelated to the effects of the substance on human health or the environment?
    If your answer to any of the above questions is yes, explain how such information would be revealed.
13. Provide the Chemical Abstract Service Registry Number for the product, if known. Is your company applying for a CAS number now or in the near future? If you have applied for a CAS number, include a copy of the contract with CAS.
14. Is the substance or any information claimed CBI the subject of FIFRA regulation or reporting? If so, explain.